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10/069,141	02/15/2002	Gerhard Hartwich	PATKRI P03AUS	7623

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/069,141	Hartwich
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 12, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3* is/are rejected.

7) ☒ Claim(s) *4-57* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. *10/069,141* .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
4) ☐ Interview Summary (PTO-413) Paper No(s). ____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claims 58 and 60 are objected to because of the following informalities: There are two periods at the end of claim 58. Claim 60 is not a correct and complete sentence. Appropriate corrections are required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 73 and 74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although it is not clear what is meant by the word "groups", for the purpose of proper examination, it is considered that groups of the periodic table is being referred to here.The specification discloses only gold metal in the working examples. Claims 73-74 are directed to encompass more than 1000 metal alloys. None of these binary and ternary metal alloys meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of gold, the skilled artisan cannot envision the detailed chemical structure of the encompassed metal alloys attached to the modified oligomer, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method or periodic table for isolating it. The metal alloy itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas,

etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

In support of this position attention is directed to the decision *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, In the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to

complete the generic invention, while In the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

***

We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

Therefore, only gold but not the full breadth of the claim (or none of the metal alloys encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

In absence of any working example In the specification, it is also not clear if the applicant had the actual possession of these compounds at the time the invention was made.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 60, 61, 73 and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 60, it is not clear if the modified nucleic acid oligomer is claimed or the single-stranded DNA, RNA, or PNA is claimed or both are claimed. In absence of a correct and complete sentence describing the claim, the metes and bounds of the claim is vague and indefinite.

Regarding claims 73 and 74, it is not clear elements of which "groups" are claimed In the instant invention. The word "group" is not disclosed clearly either In the claim or In the specification. The metes and bounds of the claims are vague and indefinite.

In absence of any working example In the specification, it is also not clear if the applicant had the actual possession of these compounds at the time the invention was made.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth In this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth In section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill In the art to which said subject matter pertains. Patentability shall not be negatived by the manner In which the invention was made.

7. Claims 58-72, and 75-86 are rejected under 35 U.S.C. 103(a) over Barton et al. (U.S. Patent 6,221,586 B1) (April 24, 2001) In view of Lee et al. (U.S. Patent 4,749,653) (June 7, 1988).

Barton et al teaches a nucleic acid oligomer modified by attaching a catalytically redox-active moiety, characterized In that the catalytically redox-active moiety is selected from redox proteins and enzymes which use prosthetic groups such as flavins or NAD (Abstract, Column 5, lines 6-44, and Column 11, lines 5-11 and Column 11, line 63 to Column 14, line 36).

Barton et al teaches a nucleic acid oligomer, wherein the catalytically redox-active moiety is covalently attached to the phosphoric-acid , carboxylic-acid, or amine groups or to a sugar of the nucleic acid oligomer backbone (Claim 3 and Column 13, lines 2-6 and Figure 1).

Barton et al teaches a nucleic acid oligomer, wherein the modified nucleic acid oligomer sequence-specifically binds single stranded DNA (Column 12, lines 30-36).

Barton et al teaches a nucleic acid oligomer, wherein the modified nucleic acid oligomer is a DNA oligomer (Examples 1-14).

Barton et al teaches a nucleic acid oligomer, wherein following attachment to the nucleic acid oligomer, the catalytically redox-active moiety possesses electrocatalytic activity (Column 12, lines 55-65).

Barton et al teaches a nucleic acid oligomer, wherein multiple catalytically redox-active moieties are attached to the nucleic acid oligomer (Figure 1).

Barton et al teaches a method of producing a modified nucleic acid oligomer, wherein, alternatively, the nucleic acid oligomer is bound to the catalytically redox-active moiety by one or more amidations with amine groups of the catalytically redox-active moiety or by thioester formation with thioalcohol groups of the catalytically redox-active moiety (Examples 1 and 3).

Barton et al teaches a method of producing a modified nucleic acid oligomer, wherein one or more branched or linear molecular moieties of any composition and chain length are covalently attached to the catalytically redox-active moiety and the branched or linear molecule moieties possess, alternatively, a reactive amine, hydroxyl, thiol, acid or aldehyde group for covalent attachment to a nucleic acid oligomer (Examples 1 and 3 and claims 3 and 7 and Figure 1).

Barton et al. teaches a method of producing a modified nucleic acid oligomer, wherein the shortest continuous link between the nucleic acid oligomer and the catalytically redox-active moiety is a branched or linear molecular moiety having a chain length of 1-20 atoms (Column 8, lines 16-19 and Figure 1).

Barton et al. teaches a modified conductive surface, wherein one or more types of modified nucleic acid oligomers are attached to a conductive surface (Figure 1 and Examples 1 and 3).

Barton et al. teaches a modified conductive surface, wherein the surface consists of a metal or semiconductor (Examples 1-14).

Barton et al. teaches a modified conductive surface, wherein the attachment of the modified nucleic acid oligomers to the conductive surface occurs covalently by chemisorption or physisorption of the phosphoric-acid , carboxylic-acid, or amine groups or to a sugar of the nucleic acid oligomer backbone (Examples 1 and 3 and Column 13, lines 35-56).

Barton et al. teaches a modified conductive surface, wherein alternatively, a reactive amine, hydroxyl, thiol, acid or aldehyde group is attached covalently or by chemisorption or physisorption to the conductive surface (Examples 1 and 3 and claims 3 and 7 and Figure 1).

Barton et al. teaches a modified conductive surface, wherein only one type of modified nucleic acid oligomer each is attached In a spatially delimited area of the conductive surface (Figures 1 and 6 and Example 11).

Barton et al. teaches a method of producing a modified conductive surface, wherein one or more types of modified nucleic acid oligomers are applied to a conductive surface and thereafter, a modification of the nucleic acid oligomers is carried out (Examples 1-14).

Barton et al. teaches a method of producing a modified conductive surface, wherein the nucleic acid oligomers are hybridized with the respective complementary nucleic acid oligomer strand and applied to the conductive surface In the form of the double-strand hybrid (Figures 1, and 5-7 and Examples 4-10).

Barton et al. teaches a method of producing a modified conductive surface, wherein the nucleic acid oligomers are applied to the conductive surface In the presence of further chemical compounds that are likewise attached to the conductive surface (Examples 1-6).

Barton et al. teaches a method of electrochemically detecting oligomer hybridization events, wherein one or more modified conductive surfaces are brought into contact with nucleic acid oligomers and, subsequently, detection of the electrical communication between the catalytically redox-active moiety and the respective conductive surface takes place (Examples Figure 5 and Examples 2, 5-8, 10-14).

Barton et al. teaches a method, wherein detection takes place by cyclic voltammetry, amperometry, potentiometry, or conductivity measurement (Example 4 and Column 8, lines 21-29).

Barton et al. teaches a method of producing a modified conductive surface, wherein electrochemical detection is initiated by adding the substrate to the catalytically redox-active moiety attached to the conductive surface via a nucleic acid oligomer (Example 4 and Column 12, lines 21-65).

Barton et al. teaches a method of producing a modified conductive surface, wherein the addition of the substrate to the catalytically redox-active moiety attached to the conductive surface via a nucleic acid oligomer is limited to an area of the conductive surface having one or more modified nucleic acid oligomer types (Example Examples 4 and 11).

Barton et al. does not teach a catalytic redox-active moiety selected from alcohol dehydrogenase, lactate dehydrogenase, and peroxidase.

Lee et al. teaches a catalytic redox-active moiety selected from alcohol dehydrogenase, lactate dehydrogenase, and peroxidase (which inherently use prosthetic groups flavins or NAD) (Column 4, line 45 to column 5, line 7).

It would have been *prima facie* obvious to one having ordinary skill In the art at the time the invention was made to substitute and combine a structurally and functionally equivalent catalytic redox-active moiety selected from redox enzymes alcohol dehydrogenase, lactate dehydrogenase, and peroxidase of Lee et al. In the modified nucleic acid oligomer of Barton et al. since Lee et al. states, "A variety of enzymes are suitable In the present invention, especially those which contain a group capable of reacting with the cross-linking agent. For example, useful enzymes may have an amino

group which is capable of reacting with an aldehyde or an isocyanate so as to be cross-linked with itself and/or the polymer (Column 4, lines 45-50) ". Moreover, further motivation is provided by Barton et al as Barton et al states, "The present invention provides a highly sensitive and accurate method based on an electrochemical assay using intercalative, redox-active species to determine the presence and location of a single or multiple base-pair mismatches (Column 11, lines 12-15)". An ordinary practitioner would have been motivated to substitute and combine a catalytic redox-active moiety selected from alcohol dehydrogenase, lactate dehydrogenase, and peroxidase of Lee et al. In the modified nucleic acid oligomer of Barton et al. In order to achieve the express advantages, as noted by Lee et al., of useful enzymes capable of reacting with an aldehyde or an isocyanate so as to be cross-linked with itself and/or the polymer and also In order to achieve the express advantages, as noted by Barton et al., of an invention which provides a highly sensitive and accurate method based on an electrochemical assay using intercalative, redox-active species to determine the presence and location of a single or multiple base-pair mismatches.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703)605-1237.

Arun Kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER

Arun Chakrabarti,

Patent Examiner,

March 31, 2003